---------<<< Arsenic, inorganic >>>---------

__IV.B. SAFE DRINKING WATER ACT (SDWA)

___IV.B.1. MAXIMUM CONTAMINANT LEVEL GOAL (MCLG) for Drinking Water

Value (status) -- 0.05 mg/L (Proposed, 1985)

Considers technological or economic feasibility? -- NO

Discussion -- An MCLG of 0.05 mg/L for arsenic is proposed based on the current MCL of 0.05 mg/L. Even though arsenic is potentially carcinogenic in humans by inhalation and ingestion, its potential essential nutrient value was considered in determination of an MCLG. The basis for this evaluation is nutritional requirements by NAS (NAS, 1983, Vol. 5, Drinking Water and Health, National Academy of Sciences Press, Washington, DC.)

Reference -- 50 FR 46936 Part IV (11/13/85)

EPA Contact -- Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

<<< Arsenic, inorganic >>>

___IV.B.2. MAXIMUM CONTAMINANT LEVEL (MCL) for Drinking Water

Value (status) -- 0.05 mg/L (Interim, 1980)

Considers technological or economic feasibility? -- YES

Discussion -- As an interim measure the U.S. EPA is using the value previously derived by the Public Health Service.

Reference -- 45 FR 57332 (08/27/80)

EPA Contact -- Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

---------<<< Arsenic, inorganic >>>---------

__IV.C. CLEAN WATER ACT (CWA)

___IV.C.1. AMBIENT WATER QUALITY CRITERIA, Human Health

Water and Fish Consumption -- 2.2E-3 ug/L

Fish Consumption Only -- 1.75E-2 ug/L

Considers technological or economic feasibility? -- NO

Discussion -- For the maximum protection from the potential carcinogenic properties of this chemical, the ambient water concentration should be zero. However, zero may not be attainable at this time, so the recommended criteria represents a E-6 estimated incremental increase of cancer risk over a lifetime.

Reference -- 45 FR 79318 (11/28/80)

EPA Contact -- Criteria and Standards Division, OWRS
(202)475-7315 / FTS 475-7315

<<< Arsenic, inorganic >>>

___IV.C.2. AMBIENT WATER QUALITY CRITERIA, Aquatic Organisms

Freshwater:

Acute -- 3.6E+2 ug/L (Arsenic III)
Chronic -- 1.9E+2 ug/L (Arsenic III)

Marine:

Acute -- 6.9E+1 ug/L (Arsenic III)
Chronic -- 3.6E+1 ug/L (Arsenic III)

Considers technological or economic feasibility? -- NO

Discussion -- The criteria given are for Arsenic III. Much less data are available on the effects of Arsenic V to aquatic organisms, but the toxicity seems to be less. A complete discussion may be found in the referenced notice.

Reference -- 50 FR 30784 (07/29/85)

EPA Contact -- Criteria and Standards Division, OWRS
(202)475-7315 / FTS 475-7315

----------<<< Arsenic, inorganic >>>----------

__IV.D. FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA)

No data available

----------<<< Arsenic, inorganic >>>----------

__IV.E. TOXIC SUBSTANCES CONTROL ACT (TSCA)

No data available

----------<<< Arsenic, inorganic >>>----------

__IV.F. RESOURCE CONSERVATION AND RECOVERY ACT (RCRA)

___IV.F.1. RCRA APPENDIX IX, for Ground Water Monitoring

Status -- Listed

Reference -- 52 FR 25942 (07/09/87)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

----------<<< Arsenic, inorganic >>>----------

__IV.G. SUPERFUND (CERCLA)

___IV.G.1. REPORTABLE QUANTITY (RQ) for Release into the Environment

Value (status) -- 1 pound (Proposed, 1987)

Considers technological or economic feasibility? -- NO

Discussion -- The proposed 1-pound RQ for arsenic is based on its potential carcinogenicity. Available data indicate a hazard ranking of high based on a potency factor of 142.31/mg/kg/day and a weight-of-evidence group A, which corresponds to an RQ of 1 pound. Evidence found in "Water-Related Environmental Fate of 129 Priority Pollutants" (EPA 440/4-79-029a) also indicates that this material, or a constituent of this material, is bioaccumulated to toxic levels in the tissue of aquatic and marine organisms, and has the potential to concentrate in the food chain.

Reference -- 52 FR 8140 (03/16/87)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

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_V. SUPPLEMENTARY DATA

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2

Not available at this time.

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_VI. BIBLIOGRAPHY

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2
Last Revised -- 06/01/90

__VI.A. ORAL RfD REFERENCES

None

----------<<< Arsenic, inorganic >>>----------

VI.B. INHALATION RfD REFERENCES

None

----------<<< Arsenic, inorganic >>>----------

VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

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Matanoski, G., E. Landau, J. Tonascia, C. Lazar, E. Elliot, W. McEnroe and K. King. 1981. Cancer mortality in an industrial area of Baltimore. Environ. Res. 25: 8-28.

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Ohno, H., F. Hanaoka and M. Yamada. 1982. Inductibility of sister chromatid exchanges by heavy-metal ions. Mutat. Res. 104: 141-145.

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----------<<< Arsenic, inorganic >>>----------

__VI.D. DRINKING WATER HA REFERENCES

None

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SYNONYMS

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2
Last Revised -- 02/10/88

7440-38-2
Arsenic
Arsenic, inorganic
gray-arsenic

Barium; CASRN 7440-39-3 (08/01/90)

Health risk assessment information on a chemical is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Program Offices. The summaries presented in Sections I and II represent a consensus reached in the review process. The other sections contain U.S. EPA information which is specific to a particular EPA program and has been subject to review procedures prescribed by that Program Office. The regulatory actions in Section IV may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of regulatory action data for a particular situation, note the date of the regulatory action, the date of the most recent risk assessment relating to that action, and whether technological factors were considered. Background information and explanations of the methods used to derive the values given in IRIS are provided in the five Background Documents in Service Code 5, which correspond to Sections I through V of the chemical files.

STATUS OF DATA FOR Barium

File On-Line 01/31/87

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	08/01/90
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	no data	
Drinking Water Health Advisories (III.A.)	no data	
U.S. EPA Regulatory Actions (IV.)	on-line	03/01/88
Supplementary Data (V.)	no data	

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I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Barium
CASRN -- 7440-39-3
Last Revised -- 08/01/90

The Reference Dose (RfD) is based on the assumption that thresholds exist for

certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to Background Document 1 in Service Code 5 for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file when a review of that evaluation is completed.

<<< Barium >>>

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Increased blood pressure	NOAEL: 10 mg/L (0.21 mg/kg/day)	3	1	7E-2 mg/kg/day
Subchronic to Chronic Human Drinking Water Studies	LOAEL: None			
Wones et al., 1990; Brenniman and Levy, 1984				

*Conversion Factors: 10 mg/L x 1.5 L/day/70 kg = 0.21 mg/kg/day

<<< Barium >>>

___I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

Wones, R.G., B.L. Stadler and L.A. Frohman. 1990. Lack of effect of drinking water barium on cardiovascular risk factor. Environ. Health Perspect. 85: 1-13.

Brenniman, G.R. and P.S. Levy. 1984. High barium levels in public drinking water and its association with elevated blood pressure. In: Advances in Modern Toxicology IX, E.J. Calabrese, Ed. Princeton Scientific Publications, Princeton NJ. p. 231-249.

No single study considered alone is appropriate to calculate a lifetime RfD for barium. The RfD must be based rather on a weight of evidence approach which takes into account recent findings of the Wones et al. (1990) and Brenniman and Levy (1984) epidemiologic studies as well as the various rodent studies that have been conducted (Perry et al., 1983; McCauley et al., 1985; Schroeder and Mitchener, 1975a,b; Tardiff et al., 1980). Because of the number of studies involved, the complete reference citations are given in the Section VI.

Wones et al. (1990) administered barium (as barium chloride) in the drinking water of 11 healthy male volunteers. Subjects ranged in age from 27 to 61 years and had no previous history of diabetes, hypertension, or cardiovascular disease. Diets were strictly controlled throughout the 10-week study. Subjects were given 1.5 L/day of distilled and charcoal-filtered water containing 0 mg/L barium for weeks 0 to 2; 5 mg/L for weeks 3 to 6, and 10 mg/L for weeks 7 to 10. Blood and urine samples, as well as morning and

evening blood pressures, were taken. Electrocardiograms and 24-hour continuous electrocardiographic monitoring were also performed.

There were no changes in systolic or diastolic blood pressures, or serum chemistry, especially total cholesterol, HDL, LDL, triglycerides, potassium or glucose levels. There was an increase in serum calcium levels that was attributed to a decrease in serum albumin levels. This increase, although statistically significant, was considered borderline and not clinically significant. There were also no changes in cardiac cycle as noted by electrocardiograms and no significant arrhythmias. A NOAEL of 10 mg/L was identified in this study which corresponds to 0.21 mg/kg/day, based on an actual consumption rate of 1.5 L/day and a 70-kg body weight.

Brenniman and Levy (1984) conducted a retrospective epidemiology study which compared human mortality and morbidity rates in populations ingesting elevated barium levels (2 to 10 mg/L) in their drinking water to populations ingesting very little or no barium (less than or equal to 0.2 mg/L). Mortality rates for cardiovascular diseases were determined for the years 1971-1975 and were age-adjusted. For the morbidity study, 1175 adult males and 1203 adult females were selected from communities in which the average drinking water concentration was 7.3 mg/L. Differences in mortality rates from all cardiovascular diseases were significantly higher ($p<0.05$) in the communities with elevated barium. However, these differences were largely in the 65 and over age group and did not account for confounding variables such as population mobility, or use of water softeners or medication.

Differences in blood pressure, prevalance of hypertension, stroke, and heart and renal disease were also measured between the individuals in the two communities. Data were analyzed using signed ranked test for age-specific rates, the weighted Z test for prevalence rates, and analysis of variance for blood pressures. No significant differences were found in mean systolic and diastolic pressures between the two communities. No significant differences were found when the total populations were broken down by duration (10 years or more), medication, or use of water softeners. Also, the prevalence rates for hypertension, stroke, and heart and kidney disease were not significantly different between the communities.

A concentration of 7.3 mg/L corresponds to a dose of 0.20 mg/kg/day (assuming a 70-kg adult drinks 2 L/day).

<<< Barium >>>

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF = 3. According to U.S. EPA guidelines, an uncertainty factor of 10 is applied when a NOAEL from a subchronic human study is employed. However, data are available from chronic human studies which support this NOAEL, as well as several oral chronic animal studies. Therefore, this UF is not considered necessary. In addition, another factor of 10 is used with a human study to protect sensitive individuals. However, the data base supports the finding that the critical effect is hypertension which results from long exposure durations, and that the population most at risk is the adult male. Furthermore, the chosen study is a careful observation of this critical effect in adult males. Because of both the critical study's unique focus and the supporting studies, a 3-fold UF, instead of a 10-fold UF, was chosen as most appropriate to protect for sensitive individuals within that population.

MF = 1.

<<< Barium >>>

___I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

Occupational studies of workers exposed to barium dust have shown that workers develop "baritosis." Affected workers showed no symptoms, no abnormal physical signs, no loss of vital capacity or interference with function, although they had a significantly higher incidence of hypertension.

McCauley et al. (1985) studied the histologic and cardiovascular effects of drinking water containing 0, 10, 100, or 250 mg/L barium for 36 weeks; 0, 1, 10, 100, or 1000 mg/L barium for 16 weeks, or 0, 10, 100, or 250 mg/L (0, 1.4, 14, 35, or 140 mg/kg Ba) barium for 68 weeks on male Sprague-Dawley rats (6/group). Females were exposed to 0 or 250 mg/L for 46 weeks. No significant histologic, carcinogenic, or cardiovascular (including hypertension) effects were observed. No changes were reported in body weight, or food and water consumption in any of the treated animals. Animals treated at the highest dose (1000 mg/L) did exhibit ultrastructural changes in the kidney glomeruli and the presence of myelin figures. No other effects were reported at any dose level for males or females.

Perry et al. (1983) exposed weanling rats to barium at 1, 10, or 100 ppm in drinking water for up to 16 months (average daily barium doses of 0.051, 0.51, and 5.1 mg/kg, respectively). There were no signs of toxicity at any barium dose level. Systolic blood pressure measurements revealed no increase in animals exposed to 1 ppm for 16 months, an increase of 4 mm Hg ($p<0.01$) in animals exposed to 10 ppm barium for 16 months, and an increase of 16 mm Hg ($p<0.001$) in animals exposed to 100 ppm barium for 16 months. The animals in this study were maintained in a special contaminant-free environment and fed a diet designed to reduce exposure to trace metals. It is possible that the restricted intake of certain beneficial metals (e.g., calcium and potassium) may have predisposed the test animals to the hypertensive effects of barium (U.S. EPA, 1985).

Schroeder and Mitchener (1975a,b) exposed rats and mice to 5 mg/L barium in drinking water for a lifetime (approximately 0.25 mg/kg/day for rats and 0.825 mg/kg/day for mice). No adverse effects were observed; however, blood pressure was not measured.

Tardiff et al. (1980) exposed rats to barium at 0, 10, 50, or 250 ppm in drinking water for 4, 8, and 13 weeks. The barium concentrations were approximately 0, 2.75, 13.7, and 66.25 mg/kg/day at the beginning of the study and 0, 1.7, 6.6, and 31.5 mg/kg/day at the end of the study. Although the barium body burden increased with increasing barium dosage, no conclusive signs of barium toxicity were observed in these animals. Blood pressure was not measured.

<<< Barium >>>

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study: Medium
Data Base: Medium
RfD: Medium

As previously stated, EPA does not believe that any single study, considered alone, is adequate to calculate an RfD for barium. However, EPA believes that medium confidence can be placed in the total data base used to determine the RfD.

<<< Barium >>>

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

Source Document -- U.S. EPA. 1985. Draft Drinking Water Health Effects Criteria Document on Barium. Office of Drinking Water, Washington, DC. NTIS PB 86-118031/AS.

Agency RfD Work Group Review: 07/08/85, 07/22/85, 12/15/87, 05/17/90, 06/21/90

Verification Date: 06/21/90

___I.A.7. EPA CONTACTS (ORAL RfD)

Kenneth L. Bailey / ODW -- (202)382-5535 / FTS 382-5535

Linda R. Papa / ODW -- (513)569-7587 / FTS 684-7587

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Barium
CASRN -- 7440-39-3

Not available at this time.

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_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Barium
CASRN -- 7440-39-3

This substance/agent has not been evaluated by the U.S. EPA for evidence of human carcinogenic potential.

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_III. HEALTH HAZARD ASSESSMENTS FOR VARIED EXPOSURE DURATIONS

___III.A. DRINKING WATER HEALTH ADVISORIES

Substance Name -- Barium
CASRN -- 7440-39-3

Not available at this time.

__III.B. OTHER ASSESSMENTS

Substance Name -- Barium
CASRN -- 7440-39-3

Content to be determined.

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_IV. U.S. EPA REGULATORY ACTIONS

Substance Name -- Barium
CASRN -- 7440-39-3
Last Revised -- 03/01/88

EPA risk assessments may be updated as new data are published and as assessment methodologies evolve. Regulatory actions are frequently not updated at the same time. Compare the dates for the regulatory actions in this section with the verification dates for the risk assessments in sections I and II, as this may explain inconsistencies. Also note that some regulatory actions consider factors not related to health risk, such as technical or economic feasibility. Such considerations are indicated for each action. In addition, not all of the regulatory actions listed in this section involve enforceable federal standards. Please direct any questions you may have concerning these regulatory actions to the U.S. EPA contact listed for that particular action. Users are strongly urged to read the background information on each regulatory action in Background Document 4 in Service Code 5.

<<< Barium >>>

__IV.A. CLEAN AIR ACT (CAA)

No data available

----------<<< Barium >>>----------

__IV.B. SAFE DRINKING WATER ACT (SDWA)

___IV.B.1. MAXIMUM CONTAMINANT LEVEL GOAL (MCLG) for Drinking Water

Value (status) -- 1.5 mg/L (Proposed, 1985)

Considers technological or economic feasibility? -- NO

Discussion -- An MCLG of 1.5 mg/L for barium is proposed based on a provisional DWEL of 1.8 mg/L. A DWEL was calculated from a LOAEL of 5.1 mg/kg/day barium for hypertensinogenic and cardiotoxic effects in rats (16-month drinking water study). An uncertainty factor of 100 (based on minimized exposure to calcium) was applied and consumption of 2 L of water/day was

assumed. Data indicate that 83% is the relative source contribution from drinking water. Data were factored in on humans (0.7 mg/day in the diet and 0 mg/day by air).

Reference -- 50 FR 46936 Part IV (11/13/85)

EPA Contact -- Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

<<< Barium >>>

___IV.B.2. MAXIMUM CONTAMINANT LEVEL (MCL) for Drinking Water

Value (status) -- 1.0 mg/L (Interim, 1980)

Considers technological or economic feasibility? -- YES

Discussion --

Reference -- 45 FR 57332

EPA Contact -- Kenneth Bailey / Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

----------<<< Barium >>>----------

__IV.C. CLEAN WATER ACT (CWA)

No data available

----------<<< Barium >>>----------

__IV.D. FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA)

No data available

----------<<< Barium >>>----------

__IV.E. TOXIC SUBSTANCES CONTROL ACT (TSCA)

No data available

----------<<< Barium >>>----------

__IV.F. RESOURCE CONSERVATION AND RECOVERY ACT (RCRA)

___IV.F.1. RCRA APPENDIX IX, for Ground Water Monitoring

Status -- Listed

Reference -- 52 FR 25942 (07/09/87)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

---------<<< Barium >>>---------

__IV.G. SUPERFUND (CERCLA)

No data available

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_V. SUPPLEMENTARY DATA

Substance Name -- Barium
CASRN -- 7440-39-3

Not available at this time.

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_VI. BIBLIOGRAPHY

Substance Name -- Barium
CASRN -- 7440-39-3
Last Revised -- 08/01/90

__VI.A. ORAL RfD REFERENCES

Brenniman, G.R. and P.S. Levy. 1984. Epidemiological study of barium in Illinois drinking water supplies. In: Advances in Modern Environmental Toxicology IX, E.J. Calabrese, R.W. Tuthill and L. Condie, Ed. Princeton Scientific Publications, Princeton NJ. p. 231-240.

McCauley, P.T., B.H. Douglas, R.D. Laurie and R.J. Bull. 1985. Investigations into the effect of drinking water barium on rats. Environ. Health Perspect. Vol. IX, E.J. Calabrese, Ed. Princeton Scientific Publications, Princeton, NJ. p. 197-210.

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Wones, R.G., B.L. Stadler and L.A. Frohman. 1990. Lack of effect of drinking water barium on cardiovascular risk factor. Environ. Health Perspect. 85: 1-13.

----------<<< Barium >>>----------

__VI.B. INHALATION RfD REFERENCES

None

----------<<< Barium >>>----------

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

None

----------<<< Barium >>>----------

__VI.D. DRINKING WATER HA REFERENCES

None

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SYNONYMS

Substance Name -- Barium
CASRN -- 7440-39-3
Last Revised -- / /

7440-39-3
Barium
UN 1399
UN 1400
UN 1854

Cadmium; CASRN 7440-43-9 (04/01/91)

Health risk assessment information on a chemical is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Program Offices. The summaries presented in Sections I and II represent a consensus reached in the review process. The other sections contain U.S. EPA information which is specific to a particular EPA program and has been subject to review procedures prescribed by that Program Office. The regulatory actions in Section IV may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of regulatory action data for a particular situation, note the date of the regulatory action, the date of the most recent risk assessment relating to that action, and whether technological factors were considered. Background information and explanations of the methods used to derive the values given in IRIS are provided in the five Background Documents in Service Code 5, which correspond to Sections I through V of the chemical files.

STATUS OF DATA FOR Cadmium

File On-Line 03/31/87

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	10/01/89
Inhalation RfC Assessment (I.B.)	pending	
Carcinogenicity Assessment (II.)	on-line	03/01/91
Drinking Water Health Advisories (III.A.)	no data	
U.S. EPA Regulatory Actions (IV.)	on-line	06/01/90
Supplementary Data (V.)	no data	

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I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Cadmium
CASRN -- 7440-43-9
Last Revised -- 10/01/89

The Reference Dose (RfD) is based on the assumption that thresholds exist for

certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to Background Document 1 in Service Code 5 for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file when a review of that evaluation is completed.

<<< Cadmium >>>

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Significant proteinuria	NOAEL (water): 0.005 mg/kg/day	10	1	5E-4 mg/kg/day (water)
Human studies involving chronic exposures	NOAEL (food): 0.01 mg/kg/day	10	1	1E-3 mg/kg/day (food)

U.S. EPA, 1985

*Conversion Factors: See text for discussion

<<< Cadmium >>>

___I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

U.S. EPA. 1985. Drinking Water Criteria Document on Cadmium. Office of Drinking Water, Washington, DC. (Final draft)

A concentration of 200 ug cadmium (Cd)/gm wet human renal cortex is the highest renal level not associated with significant proteinuria (U.S. EPA, 1985). A toxicokinetic model is available to determine the level of chronic human oral exposure (NOAEL) which results in 200 ug Cd/gm wet human renal cortex; the model assumes that 0.01% day of the Cd body burden is eliminated per day (U.S. EPA, 1985). Assuming 2.5% absorption of Cd from food or 5% from water, the toxicokinetic model predicts that the NOAEL for chronic Cd exposure is 0.005 and 0.01 mg Cd/kg/day from water and food, respectively (i.e., levels which would result in 200 ug Cd/gm wet weight human renal cortex). Thus, based on an estimated NOAEL of 0.005 mg Cd/kg/day for Cd in drinking water and an UF of 10, an RfD of 0.0005 mg Cd/kg/day (water) was calculated; an equivalent RfD for Cd in food is 0.001 mg Cd/kg/day (see Section VI.A. for references).

<<< Cadmium >>>

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF = 10. This uncertainty factor is used to account for intrahuman variability to the toxicity of this chemical in the absence of specific data on sensitive individuals.

MF = 1.

<<< Cadmium >>>

___I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

Cd is unusual in relation to most, if not all, of the substances for which an oral RfD has been determined in that a vast quantity of both human and animal toxicity data are available. The RfD is based on the highest level of Cd in the human renal cortex (i.e., the critical level) not associated with significant proteinuria (i.e., the critical effect). A toxicokinetic model has been used to determine the highest level of exposure associated with the lack of a critical effect. Since the fraction of ingested Cd that is absorbed appears to vary with the source (e.g., food vs. drinking water), it is necessary to allow for this difference in absorption when using the toxicokinetic model to determine an RfD.

<<< Cadmium >>>

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study: Not applicable
Data Base: High
RfD: High

The choice of NOAEL does not reflect the information from any single study. Rather, it reflects the data obtained from many studies on the toxicity of cadmium in both humans and animals. These data also permit calculation of pharmacokinetic parameters of cadmium absorption, distribution, metabolism and elimination. All of this information considered together gives high confidence in the data base. High confidence in either RfD follows as well.

<<< Cadmium >>>

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

U.S. EPA. 1985. Drinking Water Criteria Document on Cadmium. Office of Drinking Water, Washington, DC. (Final draft)

Agency RfD Work Group Review: 05/15/86, 08/19/86, 09/17/87, 12/15/87, 01/20/88, 05/25/88

Verification Date: 05/25/88

___I.A.7. EPA CONTACTS (ORAL RfD)

Ken Bailey / ODW -- (202)382-5535 / FTS 382-5535

Warren Banks / OWRS -- (202)382-7893 / FTS 382-7893

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Cadmium
CASRN -- 7440-43-9

A risk assessment for this substance/agent is under review by an EPA work group.

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_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Cadmium
CASRN -- 7440-43-9
Last Revised -- 03/01/91

Section II provides information on three aspects of the carcinogenic risk assessment for the agent in question; the U.S. EPA classification, and quantitative estimates of risk from oral exposure and from inhalation exposure. The classification reflects a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. Background Document 2 (Service Code 5) provides details on the rationale and methods used to derive the carcinogenicity values found in IRIS. Users are referred to Section I for information on long-term toxic effects other than carcinogenicity.

<<< Cadmium >>>

__II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

____II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- B1; probable human carcinogen

Basis -- Limited evidence from occupational epidemiologic studies of cadmium is consistent across investigators and study populations. There is sufficient evidence of carcinogenicity in rats and mice by inhalation and intramuscular and subcutaneous injection. Seven studies in rats and mice wherein cadmium salts (acetate, sulfate, chloride) were administered orally have shown no evidence of carcinogenic response.

<<< Cadmium >>>

____II.A.2. HUMAN CARCINOGENICITY DATA

Limited. A 2-fold excess risk of lung cancer was observed in cadmium smelter workers. The cohort consisted of 602 white males who had been employed in production work a minimum of 6 months during the years 1940-1969. The population was followed to the end of 1978. Urine cadmium data available for 261 workers employed after 1960 suggested a highly exposed population. The authors were able to ascertain that the increased lung cancer risk was probably not due to the presence of arsenic or to smoking (Thun et al., 1985). An evaluation by the Carcinogen Assessment Group of these possible confounding factors has indicated that the assumptions and methods used in accounting for

them may not be valid. As the SMRs observed were low and there is a lack of clear cut evidence of a causal relationship of the cadmium exposure only, this study is considered to supply only limited evidence of human carcinogenicity.

An excess lung cancer risk was also observed in three other studies which were, however, compromised by the presence of other carcinogens (arsenic, smoking) in the exposure or by a small population (Varner, 1983; Sorahan and Waterhouse, 1983; Armstrong and Kazantzis, 1983).

Four studies of workers exposed to cadmium dust or fumes provided evidence of a statistically significant positive association with prostate cancer (Kipling and Waterhouse, 1967; Lemen et al., 1976; Holden, 1980; Sorahan and Waterhouse, 1983), but the total number of cases was small in each study. The Thun et al. (1985) study is an update of an earlier study (Lemen et al., 1976) and does not show excess prostate cancer risk in these workers. Studies of human ingestion of cadmium are inadequate to assess carcinogenicity.

<<< Cadmium >>>

II.A.3. ANIMAL CARCINOGENICITY DATA

Exposure of Wistar rats to cadmium as cadmium chloride at concentrations of 12.5, 25 and 50 ug/cu.m for 18 months, with an additional 13-month observation period, resulted in significant increases in lung tumors (Takenaka et al., 1983). Intratracheal instillation of cadmium oxide did not produce lung tumors in Fischer 344 rats but rather mammary tumors in females and tumors at multiple sites in males (Sanders and Mahaffey, 1984). Injection site tumors and distant site tumors (for example, testicular) have been reported by a number of authors as a consequence of intramuscular or subcutaneous administration of cadmium metal and chloride, sulfate, oxide and sulfide compounds of cadmium to rats and mice (U.S. EPA, 1985). Seven studies in rats and mice where cadmium salts (acetate, sulfate, chloride) were administered orally have shown no evidence of a carcinogenic response.

<<< Cadmium >>>

II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

Results of mutagenicity tests in bacteria and yeast have been inconclusive. Positive responses have been obtained in mutation assays in Chinese hamster cells (Dom and V79 lines) and in mouse lymphoma cells (Casto, 1976; Ochi and Ohsawa, 1983; Oberly et al., 1982).

Conflicting results have been obtained in assays of chromosomal aberrations in human lymphocytes treated in vitro or obtained from exposed workers. Cadmium treatment in vivo or in vitro appears to interfere with spindle formation and to result in aneuploidy in germ cells of mice and hamsters (Shimada et al., 1976; Watanabe et al., 1979; Gilliavod and Leonard, 1975).

----------<<< Cadmium >>>----------

II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

Not available. There are no positive studies of orally ingested cadmium suitable for quantitation.

----------<<< Cadmium >>>----------

II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

II.C.1. SUMMARY OF RISK ESTIMATES

Inhalation Unit Risk -- 1.8E-3 per (ug/cu.m)

Extrapolation Method -- Two stage; only first affected by exposure; extra risk

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	6E-2 ug/cu.m
E-5 (1 in 100,000)	6E-3 ug/cu.m
E-6 (1 in 1,000,000)	6E-4 ug/cu.m

<<< Cadmium >>>

II.C.2. DOSE-RESPONSE DATA FOR CARCINOGENICITY, INHALATION EXPOSURE

Tumor Type -- lung, trachea, bronchus cancer deaths
Test Animals -- human/white male
Route -- inhalation, exposure in the workplace
Reference -- Thun et al., 1985

Cumulative Exposure (mg/day/cu.m)	Median Observation	24 hour/ ug/cu.m Equivalent	No. of Expected Lung, Trachea and Bronchus Cancers Assuming No Cadmium Effect	Observed No. of Deaths (lung, trachea, bronchus cancers)
less than or equal to 584	280	168	3.77	2
585-2920	1210	727	4.61	7
greater than or equal to 2921	4200	2522	2.50	7

The 24-hour equivalent = median observation x 10E-3 x 8/24 x 1/365 x 240/365.

<<< Cadmium >>>

II.C.3. ADDITIONAL COMMENTS (CARCINOGENICITY, INHALATION EXPOSURE)

The unit risk should not be used if the air concentration exceeds 6 ug/cu.m, since above this concentration the unit risk may not be appropriate.

<<< Cadmium >>>

II.C.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, INHALATION EXPOSURE)

The data were derived from a relatively large cohort. Effects of arsenic and smoking were accounted for in the quantitative analysis for cadmium

effects.

An inhalation unit risk for cadmium based on the Takenaka et al. (1983) analysis is 9.2E-2 per (ug/cu.m). While this estimate is higher than that derived from human data [1.8E-3 per (ug/cu.m)] and thus more conservative, it was felt that the use of available human data was more reliable because of species variations in response and the type of exposure (cadmium salt vs. cadmium fume and cadmium oxide).

----------<<< Cadmium >>>----------

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

U.S. EPA. 1985. Updated Mutagenicity and Carcinogenicity Assessment of Cadmium: Addendum to the Health Assessment Document for Cadmium (May 1981, EPA 600/B-B1-023). EPA 600/B-83-025F.

<<< Cadmium >>>

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

The Addendum to the Cadmium Health Assessment has received both Agency and external review.

Agency Work Group Review: 11/12/86

Verification Date: 11/12/86

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

William E. Pepelko / ORD -- (202)382-5904 / FTS 382-5904

David Bayliss / ORD -- (202)382-5726 / FTS 382-5726

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_III. HEALTH HAZARD ASSESSMENTS FOR VARIED EXPOSURE DURATIONS

__III.A. DRINKING WATER HEALTH ADVISORIES

Substance Name -- Cadmium
CASRN -- 7440-43-9

Not available at this time.

__III.B. OTHER ASSESSMENTS

Substance Name -- Cadmium
CASRN -- 7440-43-9

Content to be determined.

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_IV. U.S. EPA REGULATORY ACTIONS

Substance Name -- Cadmium
CASRN -- 7440-43-9
Last Revised -- 06/01/90

EPA risk assessments may be updated as new data are published and as assessment methodologies evolve. Regulatory actions are frequently not updated at the same time. Compare the dates for the regulatory actions in this section with the verification dates for the risk assessments in sections I and II, as this may explain inconsistencies. Also note that some regulatory actions consider factors not related to health risk, such as technical or economic feasibility. Such considerations are indicated for each action. In addition, not all of the regulatory actions listed in this section involve enforceable federal standards. Please direct any questions you may have concerning these regulatory actions to the U.S. EPA contact listed for that particular action. Users are strongly urged to read the background information on each regulatory action in Background Document 4 in Service Code 5.

<<< Cadmium >>>

__IV.A. CLEAN AIR ACT (CAA)

___IV.A.1. CAA REGULATORY DECISION

Action -- Intent to list under Section 112

Considers technological or economic feasibility? -- NO

Discussion -- Cadmium is a probable human caracinogen (IARC category 2A) and according to EPA's preliminary risk assessment from ambient air exposures, public health risks are significant (3-7 cancer cases/year and maximum lifetime individual risks of 0.003. Thus, EPA indicated that it intends to add cadmium to the list of hazardous air pollutants for which it intends to establish emission standards under section 112(b)(1)(A) of the Clean Air Act. The EPA will decide whether to add cadmium to the list only after studying possible techniques that might be used to control emissions and further assessing the public health risks. The EPA will add cadmium to the list if emission standards are warranted.

Reference -- 50 FR 42000 (10/16/85)

EPA Contact -- Emissions Standards Division, OAQPS
(919)541-5571 / FTS 629-5571

---------<<< Cadmium >>>---------

__IV.B. SAFE DRINKING WATER ACT (SDWA)

___IV.B.1. MAXIMUM CONTAMINANT LEVEL GOAL (MCLG) for Drinking Water

Value (status) -- 0.005 mg/L (Proposed, 1985)

Considers technological or economic feasibility? -- NO

Discussion -- An MCLG of 0.005 mg/L for cadmium is proposed based on a provisional DWEL of 0.018 mg/L and drinking water contribution (plus aquatic organism) of 25%. A DWEL of 0.018 mg/L was calculated from a LOAEL of 0.352 mg/day for renal toxicity in humans (calculated), with an uncertainty factor of 10 applied and consumption of 2 L of water/day assumed.

Reference -- 50 FR 46936 Part IV (11/13/85)

EPA Contact -- Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

<<< Cadmium >>>

___IV.B.2. MAXIMUM CONTAMINANT LEVEL (MCL) for Drinking Water

Value (status) -- 0.01 mg/L (Interim, 1980)

Considers technological or economic feasibility? -- YES

Discussion --

Reference -- 45 FR 57332

EPA Contact -- Kenneth Bailey / Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

---------<<< Cadmium >>>---------

__IV.C. CLEAN WATER ACT (CWA)

___IV.C.1. AMBIENT WATER QUALITY CRITERIA, Human Health

Water and Fish Consumption: 1E+1 ug/L

Fish Consumption Only: None

Considers technological or economic feasibility? -- NO

Discussion -- The criteria is the same as the existing standard for drinking water.

Reference -- 45 FR 79318 (11/28/80)

EPA Contact -- Criteria and Standards Division, OWRS (202)475-7315 / FTS 475-7315

<<< Cadmium >>>

___IV.C.2. AMBIENT WATER QUALITY CRITERIA, Aquatic Organisms

Freshwater:

Acute -- 3.9E+0 ug/L (1-hour average)
Chronic -- 1.1E+0 ug/L (4-day average)

Marine:

Acute -- 4.3E+1 ug/L (1-hour average)
Chronic -- 9.3E+0 ug/L (4-day average)

Considers technological or economic feasibility? -- NO

Discussion -- The freshwater criteria are hardness dependent. Values given here are calculated at a hardness of 100 mg/L CaCO3. A complete discussion can be found in the referenced notice.

Reference -- 50 FR 30784 (07/29/85)

EPA Contact -- Criteria and Standards Division, OWRS
(202)475-7315 / FTS 475-7315

----------<<< Cadmium >>>----------

__IV.D. FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA)

____IV.D.1. PESTICIDE ACTIVE INGREDIENT, Registration Standard

None

<<< Cadmium >>>

____IV.D.2. PESTICIDE ACTIVE INGREDIENT, Special Review

Action -- Final regulatory action - PD4 (1987)

Considers technological or economic feasibility? -- YES

Summary of regulatory action -- The basis for selection of the final regulatory option is presented in Position Document 4.

Reference -- 52 FR 31076 (08/19/87)

EPA Contact -- Special Review Branch, OPP / (703)557-7400 / FTS 557-7400

----------<<< Cadmium >>>----------

__IV.E. TOXIC SUBSTANCES CONTROL ACT (TSCA)

No data available

__IV.F. RESOURCE CONSERVATION AND RECOVERY ACT (RCRA)

___IV.F.1. RCRA APPENDIX IX, for Ground Water Monitoring

Status -- Listed

Reference -- 52 FR 25942 (07/09/87)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

----------<<< Cadmium >>>----------

__IV.G. SUPERFUND (CERCLA)

___IV.G.1. REPORTABLE QUANTITY (RQ) for Release into the Environment

Value (status) -- 10 pounds (Proposed, 1987)

Considers technological or economic feasibility? -- NO

Discussion -- The proposed RQ for cadmium is 10 pounds, based on potential carcinogenicity. Available data indicate a hazard ranking of medium, based on a potency factor of 57.87/mg/kg/day and weight-of-evidence group B1, which corresponds to an RQ of 10 pounds. Cadmium has also been found to bioaccumulate in the tissues of aquatic and marine organisms, and has the potential to concentrate in the food chain.

Reference -- 52 FR 8140 (03/16/87)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

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_V. SUPPLEMENTARY DATA

Substance Name -- Cadmium
CASRN -- 7440-43-9

Not available at this time.

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_VI. BIBLIOGRAPHY

Substance Name -- Cadmium

__VI.A. ORAL RfD REFERENCES

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Friberg, L., M. Piscator, G.F. Nordberg and T. Kjellstrom. 1974. Cadmium in the environment, 2nd ed. CRC Press, Inc., Boca Raton, FL.

Shaikh, Z.A. and J.C. Smith. 1980. Metabolism of orally ingested cadmium in humans. In: Mechanisms of Toxicity and Hazard Evaluation, B. Holmstedt et al., Ed. Elsevier Publishing Co., Amsterdam. p. 569-574.

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WHO (World Health Organization). 1972. Evaluation of certain food additives and the contaminants mercury, lead, and cadmium. Sixteenth Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series No. 505, FAO Nutrition Meetings Report Series No. 51. Geneva, Switzerland.

WHO (World Health Organization). 1984. Guidelines for drinking water quality -- recommendations. Vol. 1. Geneva, Switzerland.

----------<<< Cadmium >>>----------

__VI.B. INHALATION RfD REFERENCES

None

----------<<< Cadmium >>>----------

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

Armstrong, B.G. and G. Kazantzis. 1983. The mortality of cadmium workers. Lancet. June 25, 1983: 1425-1427.

Casto, B. 1976. Letter to Richard Troast, U.S. EPA. Enclosing mutagenicity data on cadmium chloride and cadmium acetate.

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Oberly, T., C.E. Piper and D.S. McDonald. 1982. Mutagenicty of metal salts in the L5178 Y mouse lymphoma assay. J. Toxicol. Environ. Health. 9: 367-376.

Ochi, T. and M. Ohsawa. 1983. Induction of 6-thioguanine-resistant mutants and single-strand scission DNA by cadmium chloride in cultured Chinese hamster cells. Mutat. Res. 111: 69-78.

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Shimada, T., T. Watanabe and A. Endo. 1976. Potential mutagenicity of cadmium in mammalian oocytes. Mutat. Res. 40: 389-396.

Sorahan, T. and J.A.H. Waterhouse. 1983. Mortality study of nickel-cadmium battery workers by the method of regression models in life tables. Br. J. Ind. Med. 40: 293-300.

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U.S. EPA. 1985. Updated Mutagenicity and Carcinogenicity Assessment of Cadmium. Addendum to the Health Assessment Document for Cadmium (EPA 600/B-B1-023). EPA 600/B-83-025F.

Varner, M.O. 1983. Updated epidemiologic study of cadmium smelter workers. Presented at the Fourth International Cadmium Conference. Unpublished.

Watanabe, T., T. Shimada and A. Endo. 1979. Mutagenic effects of cadmium on mammalian oocyte chromosomes. Mutat. Res. 67: 349-356.

__VI.D. DRINKING WATER HA REFERENCES

None

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SYNONYMS

Substance Name -- Cadmium
CASRN -- 7440-43-9
Last Revised -- 03/31/87

7440-43-9
C.I. 77180
Cadmium
KADMIUM

Chromium(III); CASRN 16065-83-1 (11/01/90)

Health risk assessment information on a chemical is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Program Offices. The summaries presented in Sections I and II represent a consensus reached in the review process. The other sections contain U.S. EPA information which is specific to a particular EPA program and has been subject to review procedures prescribed by that Program Office. The regulatory actions in Section IV may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of regulatory action data for a particular situation, note the date of the regulatory action, the date of the most recent risk assessment relating to that action, and whether technological factors were considered. Background information and explanations of the methods used to derive the values given in IRIS are provided in the five Background Documents in Service Code 5, which correspond to Sections I through V of the chemical files.

STATUS OF DATA FOR Chromium(III)

File On-Line 01/31/87

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	03/01/88
Inhalation RfC Assessment (I.B.)	pending	
Carcinogenicity Assessment (II.)	no data	
Drinking Water Health Advisories (III.A.)	on-line	11/01/90
U.S. EPA Regulatory Actions (IV.)	on-line	08/01/90
Supplementary Data (V.)	no data	

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I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Chromium(III)
CASRN -- 16065-83-1
Last Revised -- 03/01/88

The Reference Dose (RfD) is based on the assumption that thresholds exist for

certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to Background Document 1 in Service Code 5 for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file when a review of that evaluation is completed.

<<< Chromium(III) >>>

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
No effects observed Rat Chronic Feeding Study Ivankovic and Preussmann, 1975	NOEL: 5% Cr2O3 in diet 5 days/week for 600 feedings (1800 g/kg bw average total dose) LOAEL: none	100	10	1E+0 mg/kg/day (as an insoluble salt)

*Dose Conversion Factors & Assumptions: 1800 g Cr2O3/kg bw x 1000 mg/g x 0.6849 Cr/g Cr2O3 / 600 feeding days x 5 feeding days/7 days = 1468 mg/kg/day

<<< Chromium(III) >>>

___I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

Ivankovic, S. and R. Preussmann. 1975. Absence of toxic and carcinogenic effects after administration of high doses of chromic oxide pigment in subacute and long-term feeding experiments in rats. Food Cosmet. Toxicol. 13: 347-351.

Groups of 60 male and female rats were fed chromic oxide (Cr_2O_3) baked in bread at dietary levels of 0, 1, 2, or 5%, 5 days/week for 600 feedings (840 total days). The primary purpose of this study was to assess the carcinogenic potential of Cr_2O_3. Body weight and food consumption were monitored. The average total amounts of ingested Cr_2O_3 were given as 360, 720, and 1800 g/kg bw for the 1, 2, and 5% treatment groups, respectively. The animals were maintained on control diets following termination of exposure until they became moribund or died. All major organs were examined histologically. Other toxicologic parameters were not mentioned explicitly, but may have included some or all of those described for the accompanying subchronic study (see below). No effects due to Cr_2O_3 treatment were observed at any dose level.

Ivankovic and Preussmann (1975) also treated rats (both sexes, 12-19 rats/group) at dietary levels of 0, 2, or 5% Cr_2O_3 in bread, 5 days/week for 90 days. Food consumption and body weight were monitored. Toxicologic parameters included serum protein, bilirubin, hematology, urinalysis, organ weights, and histopathology. The only effects observed were reductions (12-37%) in the absolute weights of the livers and spleens of animals in the high-dose group. Organ weights relative to body weight were not reported. The

high dose is equivalent to 1400 mg/kg/day (dose converted using reported data).

Other subchronic oral studies show no indication of adverse effects attributable to trivalent chromium compounds, but dose levels were considerably lower.

<<< Chromium(III) >>>

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF = 100. The factor of 100 represents two 10-fold decreases in mg/kg bw/day dose that account for both the expected interhuman and interspecies variability to the toxicity of the chemical in lieu of specific data.

MF = 10. The additional modifying factor of 10 is adopted to reflect uncertainty in the NOEL because: 1) the effects observed in the 90-day study were not explicitly addressed in the 2-year study and, thus, the highest NOAEL in the 2-year study may be a LOAEL; 2) the absorption of chromium is low (<1%) and is influenced by a number of factors; thus, a considerable potential variation in absorption exists; and 3) animals were allowed to die naturally after feeding stopped (2 years) and only then was histology performed.

<<< Chromium(III) >>>

___I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

This RfD is limited to metallic chromium (III) of insoluble salts. Examples of insoluble salts include chromic III oxide (Cr203) and chromium III sulfate [Cr2(S04)3].

Very limited data suggest that Cr III may have respiratory effects on humans. No data on chronic or subchronic effects of inhaled Cr III in animals can be found. Adequate teratology data do not exist, but reproductive effects are not seen at dietary levels of 5% Cr203.

<<< Chromium(III) >>>

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study: Low
Data Base: Low
RfD: Low

The principal study is rated low because of the lack of explicit detail on study protocol and results. Low confidence in the data base reflects the lack of high-dose supporting data. The low confidence in the RfD reflects the foregoing, but also reflects the lack of an observed effect level. Thus, the RfD, as given, should be considered conservative, since the MF addresses only those factors which might lower the RfD.

<<< Chromium(III) >>>

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

U.S. EPA. 1984. Health Effects Assessment for Trivalent Chromium. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response.

The ADI in the 1984 Health Effects Assessment document received an Agency review with the help of two external scientists.

Agency RfD Work Group Review: 11/21/85, 02/05/86

Verification Date: 11/21/85

___I.A.7. EPA CONTACTS (ORAL RfD)

Michael L. Dourson / ORD -- (513)569-7544 / FTS 684-7544

Christopher T. DeRosa / ORD -- (513)569-7534 / FTS 684-7534

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Chromium(III)
CASRN -- 16065-83-1

A risk assessment for this substance/agent is under review by an EPA work group.

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_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Chromium(III)
CASRN -- 16065-83-1

This substance/agent has not been evaluated by the U.S. EPA for evidence of human carcinogenic potential.

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_III. HEALTH HAZARD ASSESSMENTS FOR VARIED EXPOSURE DURATIONS

__III.A. DRINKING WATER HEALTH ADVISORIES

Substance Name -- Chromium(III)
CASRN -- 16065-83-1
Last Revised -- 11/01/90

The Office of Drinking Water provides Drinking Water Health Advisories (HAs) as technical guidance for the protection of public health. HAs are not enforceable Federal standards. HAs are concentrations of a substance in drinking water estimated to have negligible deleterious effects in humans, when ingested, for a specified period of time. Exposure to the

substance from other media is considered only in the derivation of the lifetime HA. Given the absence of chemical-specific data, the assumed fraction of total intake from drinking water is 20%. The lifetime HA is calculated from the Drinking Water Equivalent Level (DWEL) which, in turn, is based on the Oral Chronic Reference Dose. Lifetime HAs are not derived for compounds which are potentially carcinogenic for humans because of the difference in assumptions concerning toxic threshold for carcinogenic and noncarcinogenic effects. A more detailed description of the assumptions and methods used in the derivation of HAs is provided in Background Document 3 in Service Code 5.

<<< Chromium(III) >>>

NOTE: All chromium HAs are based on total chromium (III and VI).

___III.A.1. ONE-DAY HEALTH ADVISORY FOR A CHILD

Appropriate data for calculating a One-day HA are not available. It is recommended that the Ten-day HA of 1.4 mg/L be used as the One-day HA.

<<< Chromium(III) >>>

___III.A.2. TEN-DAY HEALTH ADVISORY FOR A CHILD

Ten-day HA -- 1.4E+0 mg/L

NOAEL -- 14.4 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study)
Assumptions -- 1 L/day water consumption for a 10-kg child

Principal Study -- Gross and Heller, 1946

Rats were exposed to drinking water containing Cr(VI) (K_2CrO_4) at levels of 80 or 134 mg Cr(VI)/L for 60 days (8.3 or 14.4 mg Cr(VI)/kg/day, respectively) without adverse effects. Therefore, a NOAEL of 14.4 mg/kg/day is identified.

<<< Chromium(III) >>>

___III.A.3. LONGER-TERM HEALTH ADVISORY FOR A CHILD

Longer-term (Child) HA -- 2.4E-1 mg/L

NOAEL -- 2.4 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study)
Assumptions -- 1 L/day water consumption for a 10-kg child

Principal study -- MacKenzie et al., 1958

In a 1-year drinking water study, consumption of water containing either Cr(III) ($CrCl_3$) or Cr(VI) (K_2CrO_4) (0 to 1.87 mg/kg/day for male rats and 0 to 2.41 mg/kg/day for female rats) produced no significant differences in weight gain, appearance, or pathological changes in the blood or other tissue. Therefore, a NOAEL of 2.41 mg/kg/day is identified.

<<< Chromium(III) >>>

___III.A.4. LONGER-TERM HEALTH ADVISORY FOR AN ADULT

Longer-term (Adult) HA -- 8.4E-1 mg/L

NOAEL -- 2.4 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study)
Assumptions -- 2 L/day water consumption for a 70-kg adult

Principal study -- MacKenzie et al., 1958 (study described in III.A.3.)

<<< Chromium(III) >>>

___III.A.5. DRINKING WATER EQUIVALENT LEVEL / LIFETIME HEALTH ADVISORY

DWEL -- 1.7E-1 mg/L

Assumptions -- 2 L/day water consumption for a 70-kg adult

RfD Verification Date = 02/05/86 (see Section I.A. of this file)

Lifetime HA -- 1.2E-1 mg/L

Assumptions -- 71% exposure by drinking water

Principal study -- MacKenzie et al., 1958 (This study was used in the derivation of the chronic oral RfD; see Section I.A.2.)

<<< Chromium(III) >>>

___III.A.6. ORGANOLEPTIC PROPERTIES

No data available

<<< Chromium(III) >>>

___III.A.7. ANALYTICAL METHODS FOR DETECTION IN DRINKING WATER

Determination of chromium is by an atomic absorption technique using either direct aspiration into a flame or a furnace.

<<< Chromium(III) >>>

___III.A.8. WATER TREATMENT

The treatment technologies that are available to remove chromium from water include coagulation/filtration, lime softening, ion exchange, and reverse osmosis.

<<< Chromium(III) >>>

___III.A.9. DOCUMENTATION AND REVIEW OF HAs

U.S. EPA. 1985. Draft of the Drinking Water Criteria Document on Chromium. Office of Drinking Water, Washington, DC.

EPA review of HAs in 1985.

Public review of HAs following notification of availability in October, 1985.

Scientific Advisory Panel review of HAs in January, 1986.

Preparation date of this IRIS summary -- 06/22/87

___III.A.10. EPA CONTACTS

Kenneth Bailey / ODW -- (202)382-5535 / FTS 382-5535

Edward V. Ohanian / ODW -- (202)382-7571 / FTS 382-7571

__III.B. OTHER ASSESSMENTS

Substance Name -- Chromium(III)
CASRN -- 16065-83-1

Content to be determined.

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_IV. U.S. EPA REGULATORY ACTIONS

Substance Name -- Chromium(III)
CASRN -- 16065-83-1
Last Revised -- 08/01/90

EPA risk assessments may be updated as new data are published and as assessment methodologies evolve. Regulatory actions are frequently not updated at the same time. Compare the dates for the regulatory actions in this section with the verification dates for the risk assessments in sections I and II, as this may explain inconsistencies. Also note that some regulatory actions consider factors not related to health risk, such as technical or economic feasibility. Such considerations are indicated for each action. In addition, not all of the regulatory actions listed in this section involve enforceable federal standards. Please direct any questions you may have concerning these regulatory actions to the U.S. EPA contact listed for that particular action. Users are strongly urged to read the background information on each regulatory action in Background Document 4 in Service Code 5.

<<< Chromium(III) >>>

__IV.A. CLEAN AIR ACT (CAA)

No data available

---------<<< Chromium(III) >>>---------

__IV.B. SAFE DRINKING WATER ACT (SDWA)

___IV.B.1. MAXIMUM CONTAMINANT LEVEL GOAL (MCLG) for Drinking Water

Value (status) -- 0.12 mg/L [total chromium] (Proposed, 1985)

Considers technological or economic feasibility? -- NO

Discussion -- An MCLG of 0.12 mg/L for total chromium (Cr III and Cr VI) is proposed based on a provisional DWEL of 0.17 mg/L with data on human exposure factored in (0.10 mg/day in the diet and 0 mg/day by air). A DWEL of 0.17 mg/L was calculated from a NOAEL of 2.41 mg/kg/day in rats [1-year drinking water study (Cr VI)], with an uncertainty factor of 500 applied and consumption of 2 L of water/day assumed.

Reference -- 50 FR 46936 Part IV (11/13/85)

EPA Contact -- Kenneth Bailey / Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

<<< Chromium(III) >>>

___IV.B.2. MAXIMUM CONTAMINANT LEVEL (MCL) for Drinking Water

Value (status) -- 0.05 mg/L [total chromium] (Interim, 1980)

Considers technological or economic feasibility? -- NO

Discussion --

Reference -- 45 FR 57332

EPA Contact -- Kenneth Bailey / Criteria and Standards Division, ODW / (202)382-7571 / FTS 382-7571; or Drinking Water Hotline / (800)426-4791

----------<<< Chromium(III) >>>----------

__IV.C. CLEAN WATER ACT (CWA)

___IV.C.1. AMBIENT WATER QUALITY CRITERIA, Human Health

Water and Fish Consumption: 1.7E+5 ug/L

Fish Consumption Only: 3.433E+6 ug/L

Considers technological or economic feasibility? -- NO

Discussion -- The WQC of 1.7E+5 ug/L is based on consumption of contaminated aquatic organisms and water. A WQC of 3.433E+6 ug/L has also been established based on consumption of contaminated aquatic organisms alone.

Reference -- 45 FR 79318 (11/28/80)

EPA Contact -- Criteria and Standards Division, OWRS (202)475-7315 / FTS 475-7315

<<< Chromium(III) >>>

___IV.C.2. AMBIENT WATER QUALITY CRITERIA, Aquatic Organisms

Freshwater:

Acute -- 9.8E+2 ug/L (hardness dependent)
Chronic -- 1.2E+2 ug/L (hardness dependent)

Marine: None

Considers technological or economic feasibility? -- NO

Discussion -- For freshwater aquatic life the concentration (in ug/L) of total recoverable trivalent chromium should not exceed the numerical value given by the equations "e**(0.8190 [ln (hardness)]+3.688)" for acute exposure and "e**(0.8190 [ln (hardness)]+1.561)" for chronic exposure (** indicates exponentiation; hardness is in mg/L). For example, at a hardness of 50 mg/L, the acute and chronic WQC would be 980 and 120 ug/L, respectively.

Reference -- 50 FR 30784 (07/29/85)

EPA Contact -- Criteria and Standards Division, OWRS
(202)475-7315 / FTS 475-7315

---------<<< Chromium(III) >>>---------

__IV.D. FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA)

No data available

---------<<< Chromium(III) >>>---------

__IV.E. TOXIC SUBSTANCES CONTROL ACT (TSCA)

No data available

---------<<< Chromium(III) >>>---------

__IV.F. RESOURCE CONSERVATION AND RECOVERY ACT (RCRA)

___IV.F.1. RCRA APPENDIX IX, for Ground Water Monitoring

Status -- Listed

Reference -- 52 FR 25942 (07/09/87)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

---------<<< Chromium(III) >>>---------

__IV.G. SUPERFUND (CERCLA)

___IV.G.1. REPORTABLE QUANTITY (RQ) for Release into the Environment

Value (status) -- See discussion (Final, 1985)

Considers technological or economic feasibility? -- NO

Discussion -- Though "Chromium (III), insoluble salts" is not specifically designated as a CERCLA hazardous substance, insoluble chromium (III) salts would be considered hazardous substances under the CERCLA broad generic listing for "Chromium and Compounds." There is no corresponding reportable quantity (RQ) for this generic class of compounds. However, the releaser is still liable for cleanup costs if the designated Federal On-Scene Coordinator (OSC) decides to take response action with respect to the release of an insoluble chromium (III) salt that is not otherwise specifically listed as a CERCLA hazardous substance. There are two chromium (III) salts which are specifically listed as CERCLA hazardous substances, chromic acetate and chromic sulfate. Both have been assigned final RQs of 1000 pounds based on aquatic toxicity (as established under section 311(b)(4) of the Clean Water Act).

Reference -- 51 FR 34534 (09/29/86)

EPA Contact -- RCRA/Superfund Hotline
(800)424-9346 / (202)382-3000 / FTS 382-3000

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_V. SUPPLEMENTARY DATA

Substance Name -- Chromium(III)
CASRN -- 16065-83-1

Not available at this time.

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_VI. BIBLIOGRAPHY

Substance Name -- Chromium(III)
CASRN -- 16065-83-1
Last Revised -- 08/01/89

__VI.A. ORAL RfD REFERENCES

Ivankovic, S. and R. Preussmann. 1975. Absence of toxic and carcinogenic effects after administration of high doses of chromic oxide pigment in subacute and long-term feeding experiments in rats. Food Cosmet. Toxicol. 13: 347-351.

U.S. EPA. 1984. Health Effects Assessment for Trivalent Chromium. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH. OHEA for

the Office of Solid Waste and Emergency Response, Washington, DC.

----------<<< Chromium(III) >>>----------

__VI.B. INHALATION RfD REFERENCES

None

----------<<< Chromium(III) >>>----------

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

None

----------<<< Chromium(III) >>>----------

__VI.D. DRINKING WATER HA REFERENCES

Gross, W.G., and V.G. Heller. 1946. Chromates in animal nutrition. J. Ind. Hyg. Toxicol. 28: 52-56.

MacKenzie, R.D., R.U. Byerrum, C.F. Decker, C.A. Hoppert and R.F. Langham. 1958. Chronic toxicity studies. II. Hexavalent and trivalent chromium administered in drinking water to rats. Am. Med. Assoc. Arch. Ind. Health. 18: 232-234.

U.S. EPA. 1985. Draft of the Drinking Water Criteria Document on Chromium. Office of Drinking Water, Washington, DC.

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SYNONYMS

Substance Name -- Chromium(III)
CASRN -- 16065-83-1
Last Revised -- 01/31/87

16065-83-1
CHROMIC ION
CHROMIUM
Chromium(III)
CHROMIUM (III) ION
CHROMIUM, ION

Chromium(VI); CASRN 7440-47-3 (03/01/91)

Health risk assessment information on a chemical is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Program Offices. The summaries presented in Sections I and II represent a consensus reached in the review process. The other sections contain U.S. EPA information which is specific to a particular EPA program and has been subject to review procedures prescribed by that Program Office. The regulatory actions in Section IV may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of regulatory action data for a particular situation, note the date of the regulatory action, the date of the most recent risk assessment relating to that action, and whether technological factors were considered. Background information and explanations of the methods used to derive the values given in IRIS are provided in the five Background Documents in Service Code 5, which correspond to Sections I through V of the chemical files.

STATUS OF DATA FOR Chromium(VI)

File On-Line 03/31/87

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	03/01/88
Inhalation RfC Assessment (I.B.)	pending	
Carcinogenicity Assessment (II.)	on-line	03/01/91
Drinking Water Health Advisories (III.A.)	on-line	03/01/88
U.S. EPA Regulatory Actions (IV.)	on-line	06/01/90
Supplementary Data (V.)	no data	

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I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Chromium(VI)
CASRN -- 7440-47-3
Last Revised -- 03/01/88

The Reference Dose (RfD) is based on the assumption that thresholds exist for

certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to Background Document 1 in Service Code 5 for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file when a review of that evaluation is completed.

<<< Chromium(VI) >>>

___I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
No effects reported Rat, 1-Year Drinking Study MacKenzie et al., 1958	NOAEL: 25 mg/L of chromium as K2CrO4 (converted to 2.4 mg of chromium(VI)/kg/day) LOAEL: none	500	1	5E-3 mg/kg/day

*Dose Conversion Factors & Assumptions: Drinking water consumption = 0.097 L/kg/day (reported)

<<< Chromium(VI) >>>

___I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

MacKenzie, R.D., R.U. Byerrum, C.F. Decker, C.A. Hoppert and R.F. Langham. 1958. Chronic toxicity studies. II. Hexavalent and trivalent chromium administered in drinking water to rats. Am. Med. Assoc. Arch. Ind. Health. 18: 232-234.

Groups of eight male and eight female Sprague-Dawley rats were supplied with drinking water containing 0-11 ppm (0-11 mg/L) hexavalent chromium (as K2CrO4) for 1 year. The control group (10/sex) received distilled water. A second experiment involved three groups of 12 males and 9 female rats. One group was given 25 ppm (25 mg/L) chromium (as K2CrO4); a second received 25 ppm chromium in the form of chromic chloride; and the controls again received distilled water. No significant adverse effects were seen on appearance, weight gain, or food consumption, and there were no pathologic changes in the blood or other tissues in any treatment group. The rats receiving 25 ppm of chromium (as K2CrO4) showed an approximate 20% reduction in water consumption. This dose corresponds to 2.4 mg chromium(VI)/kg/day based on actual body weight and water consumption data.

For rats treated with 0-11 ppm (in the diet), blood was examined monthly, and tissues (livers, kidneys and femurs) were examined at 6 months and 1 year. Spleens were also examined at 1 year. The 25 ppm groups (and corresponding controls) were examined similarly, except that no animals were killed at 6 months. An abrupt rise in tissue chromium concentrations was noted in rats treated with greater than 5 ppm. The authors stated that "apparently, tissues can accumulate considerable quantities of chromium before pathological changes result." In the 25 ppm treatment groups, tissue concentrations of chromium

were approximately 9 times higher for those treated with hexavalent chromium than for the trivalent group.

Similar no-effect levels have been observed in dogs and humans. Anwar et al. (1961) observed no significant effects in female dogs (2/dose group) given up to 11.2 ppm chromium(VI) (as K2CrO4) in drinking water for 4 years. The calculated doses were 0.012-0.30 mg/kg of chromium(VI). In humans, no adverse health effects were detected (by physical examination) in a family of four persons who drank for 3 years from a private well containing chromium(VI) at approximately 1 mg/L (0.03 mg/kg/day for a 70-kg human).

<<< Chromium(VI) >>>

___I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF = 500. The uncertainty factor of 500 represents two 10-fold decreases in dose to account for both the expected interhuman and interspecies variability in the toxicity of the chemical in lieu of specific data, and an additional factor of 5 to compensate for the less-than-lifetime exposure duration of the principal study.

MF = 1

<<< Chromium(VI) >>>

___I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

This RfD is limited to metallic chromium(VI) of soluble salts. Examples of soluble salts include potassium dichromate (K2CR207), sodium dichromate (Na2Cr207), potassium chromate (K2CrO4) and sodium chromate (Na2CrO4).

Trivalent chromium is an essential nutrient. There is some evidence to indicate that hexavalent chromium is reduced in part to trivalent chromium in vivo (Petrilli and DeFlora, 1977, 1978; Gruber and Jennette, 1978).

The literature available on possible fetal damage caused by chromium compounds is limited. No studies were located on teratogenic effects resulting from ingestion of chromium.

<<< Chromium(VI) >>>

___I.A.5. CONFIDENCE IN THE ORAL RfD

Study: Low
Data Base: Low
RfD: Low

Confidence in the chosen study is low because of the small number of animals tested, the small number of parameters measured and the lack of toxic effect at the highest dose tested. Confidence in the data base is low because the supporting studies are of equally low quality, and teratogenic and reproductive endpoints are not well studied. Low confidence in the RfD follows.

<<< Chromium(VI) >>>

___I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

U.S. EPA. 1984. Health Effects Assessment for Hexavalent Chromium. Prepared by the Office of Health and Environmental Assessment, Environmental

Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1985. Drinking Water Health Advisory for Chromium. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. (Draft)

Agency RfD Work Group Review: 11/21/85, 02/05/86

Verification Date: 02/05/86

____I.A.7. EPA CONTACTS (ORAL RfD)

Kenneth L. Bailey / ODW -- (202)382-5535 / FTS 382-5535

Christopher T. DeRosa / ORD -- (513)569-7534 / FTS 684-7534

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Chromium(VI)
CASRN -- 7440-47-3

A risk assessment for this substance/agent is under review by an EPA work group.

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_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Chromium(VI)
CASRN -- 7440-47-3
Last Revised -- 03/01/91

Section II provides information on three aspects of the carcinogenic risk assessment for the agent in question; the U.S. EPA classification, and quantitative estimates of risk from oral exposure and from inhalation exposure. The classification reflects a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. Background Document 2 (Service Code 5) provides details on the rationale and methods used to derive the carcinogenicity values found in IRIS. Users are referred to Section I for information on long-term toxic effects other than carcinogenicity.

<<< Chromium(VI) >>>

II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- A; human carcinogen

Basis -- Results of occupational epidemiologic studies of chromium-exposed workers are consistent across investigators and study populations. Dose-response relationships have been established for chromium exposure and lung cancer. Chromium-exposed workers are exposed to both chromium III and chromium VI compounds. Because only chromium VI has been found to be carcinogenic in animal studies, however, it was concluded that only chromium VI should be classified as a human carcinogen.

<<< Chromium(VI) >>>

II.A.2. HUMAN CARCINOGENICITY DATA

Sufficient. Epidemiologic studies of chromate production facilities in the United States (Machle and Gregorius, 1948; Brinton et al., 1952; Mancuso and Hueper, 1951, Mancuso, 1975; Baetjer, 1950; Taylor, 1966; Enterline, 1974; Hayes et al., 1979; Hill and Ferguson, 1979), Great Britain (Bidstrup, 1951; Bidstrup and Case, 1956; Alderson et al., 1981), Japan (Watanabe and Fukuchi, 1975; Ohsaki et al., 1978; Sano and Mitohara, 1978; Satoh et al., 1981) and West Germany (Korallus et al., 1982; Bittersohl, 1971) have established an association between chromium (Cr) exposure and lung cancer. Most of these studies did not attempt to determine whether Cr III or Cr VI compounds were the etiologic agents.

Three studies of the chrome pigment industry, one in Norway (Langard and Norseth, 1975), one in England (Davies, 1978, 1979), and the third in the Netherlands and Germany (Frentzel-Beyme, 1983) also found an association between occupational chromium exposure (predominantly to Cr VI) and lung cancer.

Results of two studies of the chromium plating industry (Royle, 1975; Silverstein et al., 1981) were inconclusive, while the findings of a Japanese study of chrome platers were negative (Okubo and Tsuchiya, 1979). The results of studies of ferrochromium workers (Pokrovskaya and Shabynina, 1973; Langard et al., 1980; Axelsson et al., 1980) were inconclusive as to lung cancer risk.

<<< Chromium(VI) >>>

II.A.3. ANIMAL CARCINOGENICITY DATA

Sufficient. Hexavalent chromium compounds were carcinogenic in animal assays producing the following tumor types: intramuscular injection site tumors in Fischer 344 and Bethesda Black rats and in C57BL mice (Furst et al., 1976; Maltoni, 1974, 1976; Payne, 1960; Heuper and Payne, 1959); intrapleural implant site tumors for various chromium VI compounds in Sprague-Dawley and Bethesda Black rats (Payne, 1960; Heuper 1961; Heuper and Payne, 1962); intrabronchial implantation site tumors for various Cr VI compounds in Wistar rats (Levy and Martin, 1983; Laskin et al., 1970; Levy as quoted in NIOSH, 1975); and subcutaneous injection site sarcomas in Sprague-Dawley rats (Maltoni, 1974, 1976).

<<< Chromium(VI) >>>

II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

A large number of chromium compounds have been assayed in in vitro genetic toxicology assays. In general, hexavalent chromium is mutagenic in bacterial assays whereas trivalent chromium is not (Lofroth, 1978; Petrellie and Flora, 1977, 1978). Likewise Cr VI but not Cr III was mutagenic in yeasts (Bonatti et al., 1976) and in V79 cells (Newbold et al., 1979). Chromium III and VI compounds decrease the fidelity of DNA synthesis in vitro (Loeb et al., 1977), while Cr VI compounds inhibit replicative DNA synthesis in mammalian cells (Levis et al., 1978) and produce unscheduled DNA synthesis, presumably repair synthesis, as a consequence of DNA damage (Raffetto, 1977). Chromate has been shown to transform both primary cells and cell lines (Fradkin et al., 1975; Tsuda and Kato, 1977; Casto et al., 1979). Chromosomal effects produced by treatment with chromium compounds have been reported by a number of authors; for example, both Cr VI and Cr III salts were clastogenic for cultured human leukocytes (Nakamuro et al., 1978).

There are no long-term studies of ingested Cr VI. There appears to be significant in vivo conversion of Cr VI to Cr III and III to VI; Cr III is an essential trace element.

----------<<< Chromium(VI) >>>----------

II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

Not available.

----------<<< Chromium(VI) >>>----------

II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

II.C.1. SUMMARY OF RISK ESTIMATES

Inhalation Unit Risk -- 1.2E-2 per (ug/cu.m)

Extrapolation Method -- Multistage, extra risk

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	8E-3 ug/cu.m
E-5 (1 in 100,000)	8E-4 ug/cu.m
E-6 (1 in 1,000,000)	8E-5 ug/cu.m

<<< Chromium(VI) >>>

II.C.2. DOSE-RESPONSE DATA FOR CARCINOGENICITY, INHALATION EXPOSURE

Species/Strain Tumor Type	Dose	Tumor Incidence	Reference
human	Route: Occupational exposure		

(inhalation)

Age (years)	Midrange (ug/cu.m)	Deaths from Lung Cancer	Person Years	
50	5.66	3	1345	Mancuso,
	25.27	6	931	1975
	46.83	6	299	
60	4.68	4	1063	
	20.79	5	712	
	39.08	5	211	
70	4.41	2	401	
	21.29	4	345	

<<< Chromium(VI) >>>

___II.C.3. ADDITIONAL COMMENTS (CARCINOGENICITY, INHALATION EXPOSURE)

The cancer mortality in Mancuso (1975) was assumed to be due to Cr VI, which was further assumed to be no less than one-seventh of total chromium. It was also assumed that the smoking habits of chromate workers were similar to those of the U.S. white male population. The unit risks of Langard et al. (1980), Axelsson et al. (1980), and Pokrovskaya and Shabynina (1973) are 1.3E-1, 3.5E-2 and 9.2E-2 per (ug/cu.m), respectively.

Hexavalent chromium compounds have not produced lung tumors in animals by inhalation. Trivalent chromium compounds have not been reported as carcinogenic by any route of administration.

The unit risk should not be used if the air concentration exceeds 8E-1 ug/cu.m, since above this concentration the unit risk may not be appropriate.

<<< Chromium(VI) >>>

___II.C.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, INHALATION EXPOSURE)

Results of studies of chromium exposure are consistent across investigators and countries. A dose-relationship for lung tumors has been established. The assumption that the ratio of Cr III to Cr VI is 6:1 may lead to a 7-fold underestimation of risk. The use of 1949 hygiene data, which may underestimate worker exposure, may result in an overestimation of risk. Further overestimation of risk may be due to the implicit assumption that the smoking habits of chromate workers were similar to those of the general white male population, since it is generally accepted that the proportion of smokers is higher for industrial workers than for the general population.

----------<<< Chromium(VI) >>>----------

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

___II.D.1. EPA DOCUMENTATION

Mancuso, T.F. 1975. International Conference on Heavy Metals in the Environment. Toronto, Ontario, Canada.

U.S. EPA. 1984. Health Assessment Document for Chromium. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria

and Assessment Office, Cincinnati, OH. EPA 600/8-83-014F.

<<< Chromium(VI) >>>

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

The quantification of cancer risk in the 1984 Health Assessment Document has received peer review in public sessions of the Environmental Health Committee of the U.S. EPA's Science Advisory Board.

Agency Work Group Review: 06/26/86

Verification Date: 06/26/86

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

Herman J. Gibb / ORD -- (202)382-5898 / FTS 382-5898

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_III. HEALTH HAZARD ASSESSMENTS FOR VARIED EXPOSURE DURATIONS

___III.A. DRINKING WATER HEALTH ADVISORIES

Substance Name -- Chromium(VI)
CASRN -- 7440-47-3
Last Revised -- 03/01/88

The Office of Drinking Water provides Drinking Water Health Advisories (HAs) as technical guidance for the protection of public health. HAs are not enforceable Federal standards. HAs are concentrations of a substance in drinking water estimated to have negligible deleterious effects in humans, when ingested, for a specified period of time. Exposure to the substance from other media is considered only in the derivation of the lifetime HA. Given the absence of chemical-specific data, the assumed fraction of total intake from drinking water is 20%. The lifetime HA is calculated from the Drinking Water Equivalent Level (DWEL) which, in turn, is based on the Oral Chronic Reference Dose. Lifetime HAs are not derived for compounds which are potentially carcinogenic for humans because of the difference in assumptions concerning toxic threshold for carcinogenic and noncarcinogenic effects. A more detailed description of the assumptions and methods used in the derivation of HAs is provided in Background Document 3 in Service Code 5.

<<< Chromium(VI) >>>

NOTE: All chromium HAs are based on total chromium (III and VI).

____III.A.1. ONE-DAY HEALTH ADVISORY FOR A CHILD

Appropriate data for calculating a One-day HA are not available. It is

recommended that the Ten-day HA of 1.4 mg/L be used as the One-day HA.

<<< Chromium(VI) >>>

___III.A.2. TEN-DAY HEALTH ADVISORY FOR A CHILD

Ten-day HA -- 1.4E+0 mg/L

NOAEL -- 14.4 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study)
Assumptions -- 1 L/day water consumption for a 10-kg child

Principal Study -- Gross and Heller, 1946

Rats were exposed to drinking water containing Cr(VI) (K_2CrO_4) at levels of 80 or 134 mg Cr(VI)/L for 60 days (8.3 or 14.4 mg Cr(VI)/kg/day, respectively) without adverse effects. Therefore, a NOAEL of 14.4 mg/kg/day is identified.

<<< Chromium(VI) >>>

___III.A.3. LONGER-TERM HEALTH ADVISORY FOR A CHILD

Longer-term (Child) HA -- 2.4E-1 mg/L

NOAEL -- 2.4 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study)
Assumptions -- 1 L/day water consumption for a 10-kg child

Principal study -- MacKenzie et al., 1958

In a 1-year drinking water study, consumption of water containing either Cr(III) ($CrCl_3$) or Cr(VI) (K_2CrO_4) (0 to 1.87 mg/kg/day for male rats and 0 to 2.41 mg/kg/day for female rats) produced no significant differences in weight gain, appearance, or pathological changes in the blood or other tissue. Therefore, a NOAEL of 2.41 mg/kg/day is identified.

<<< Chromium(VI) >>>

___III.A.4. LONGER-TERM HEALTH ADVISORY FOR AN ADULT

Longer-term (Adult) HA -- 8.4E-1 mg/L

NOAEL -- 2.4 mg/kg/day
UF -- 100 (allows for interspecies and intrahuman variability with the use of a NOAEL from an animal study)
Assumptions -- 2 L/day water consumption for a 70-kg adult

Principal study -- MacKenzie et al., 1958 (study described in III.A.3.)

<<< Chromium(VI) >>>

___III.A.5. DRINKING WATER EQUIVALENT LEVEL / LIFETIME HEALTH ADVISORY

DWEL -- 1.7E-1 mg/L

Assumptions -- 2 L/day water consumption for a 70-kg adult

RfD Verification Date = 02/05/86 (see Section I.A. of this file)

Lifetime HA -- 1.2E-1 mg/L

Assumptions -- 71% exposure by drinking water

Principal study -- MacKenzie et al., 1958 (This study was used in the derivation of the chronic oral RfD; see Section I.A.2.)

<<< Chromium(VI) >>>

___III.A.6. ORGANOLEPTIC PROPERTIES

No data available

<<< Chromium(VI) >>>

___III.A.7. ANALYTICAL METHODS FOR DETECTION IN DRINKING WATER

Determination of chromium is by an atomic absorption technique using either direct aspiration into a flame or a furnace.

<<< Chromium(VI) >>>

___III.A.8. WATER TREATMENT

The treatment technologies that are available to remove chromium from water include coagulation/filtration, lime softening, ion exchange, and reverse osmosis.

<<< Chromium(VI) >>>

___III.A.9. DOCUMENTATION AND REVIEW OF HAs

U.S. EPA. 1985. Draft of the Drinking Water Criteria Document on Chromium. Office of Drinking Water, Washington, DC.

EPA review of HAs in 1985.

Public review of HAs following notification of availability in October, 1985.

Scientific Advisory Panel review of HAs in January, 1986.

Preparation date of this IRIS summary -- 06/22/87

___III.A.10. EPA CONTACTS

Kenneth Bailey / ODW -- (202)382-5535 / FTS 382-5535

Edward V. Ohanian / ODW -- (202)382-7571 / FTS 382-7571

___III.B. OTHER ASSESSMENTS

Substance Name -- Chromium(VI)